SEQUENCE LISTING

(1) GENERAL INFORMATION:

- (i) APPLICANT: Freeman, Gordon J. Nadler, Lee M. Gray, Gary S.
- (ii) TITLE OF INVENTION: TUMOR CELLS MODIFIED TO EXPRESS B7-2 AND B7-3 WITH INCREASED IMMUNOGENICITY AND USES THEREFOR
- (iii) NUMBER OF SEQUENCES: 8
- (iv) CORRESPONDENCE ADDRESS:
 - (A) ADDRESSEE: LAHIVE & COCKFIELD
 - (B) STREET: 60 State Street, Suite 510
 - (C) CITY: Boston
 - (D) STATE: Massachusetts
 - (E) COUNTRY: USA
 - (F) ZIP: 02109
- (v) COMPUTER READABLE FORM:
 - (A) MEDIUM TYPE: Floppy disk
 - (B) COMPUTER: IBM PC compatible
 - (C) OPERATING SYSTEM: PC-DOS/MS-DOS
 - (D) SOFTWARE: PatentIn Release #1.0, Version #1.25
- (vi) CURRENT APPLICATION DATA:
 - (A) APPLICATION NUMBER:
 - (B) FILING DATE:
 - (C) CLASSIFICATION:
- (vii) PRIOR APPLICATION DATA:
 - (A) APPLICATION NUMBER: 08/101,624;
 - (B) FILING DATE: 26-JUL-1993;
 - (A) APPLICATION NUMBER: 08/109,393;
 - (b) FILING DATE: 19-AUG-1993
- (viii) ATTORNEY/AGENT INFORMATION:
 - (A) NAME: Mandragouras, Amy E.
 - (B) REGISTRATION NUMBER: 36,207
 - (C) REFERENCE/DOCKET NUMBER: RPI-008
 - (ix) TELECOMMUNICATION INFORMATION:
 - (A) TELEPHONE: (617) 227-7400
 - (B) TELEFAX: (617) 227-5941

(2) INFORMATION FOR SEQ ID NO:1:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 1120 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: cDNA
- (ix) FEATURE:
 - (A) NAME/KEY: CDS
 - (B) LOCATION: 107..1093
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:1:

CACAGGGTGA AAG	SCTTTGCT TCTCTGCTG	C TGTAACAGGG	ACTAGCACAG ACACA	ACGGAT 60
GAGTGGGGTC ATT	TTCCAGAT ATTAGGTCA	C AGCAGAAGCA	GCCAAA ATG GAT C Met Asp E 1	
	rg gga CTG AGT AAC et Gly Leu Ser Asn 10			
	CT GCT CCT CTG AAG la Ala Pro Leu Lys 25			
	CA TGC CAA TTT GCA co Cys Gln Phe Ala 40			
Glu Leu Val Va	TA TTT TGG CAG GAC al Phe Trp Gln Asp 55			
	GC AAA GAG AAA TTT Ly Lys Glu Lys Phe 75	Asp Ser Val		- ·
	GT TTT GAT TCG GAC er Phe Asp Ser Asp 90			
	AG GAC AAG GGC TTG /s Asp Lys Gly Leu 105			
	GA ATG ATT CGC ATC Ly Met Ile Arg Ile 120			
	AC TTC AGT CAA CCT an Phe Ser Gln Pro 35			
	TG TAC ATA AAT TTG al Tyr Ile Asn Leu			

	150			155					160				
			AGT Ser 170									6	43
			ATG Met									6	91
			AGC Ser									7	39
			TGT Cys						-		 	7	87
			ATA Ile									8	35
			ACA Thr 250									8	83
			ATT Ile									9	31
			TGT Cys									9	79
			AGA Arg									10	27
			TTT Phe									10	75
AGT Ser 325			TAAT	XAAT'I	AGA (KAAT	AGCCC	CA AA	LAAA	AA.		11.	20

(3) INFORMATION FOR SEQ ID NO:2:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 329 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:2:

Met Asp Pro Gln Cys Thr Met Gly Leu Ser Asn Ile Leu Phe Val Met 1 5 10 15

Ala Phe Leu Leu Ser Gly Ala Ala Pro Leu Lys Ile Gln Ala Tyr Phe

Asn	Glu	Thr 35	Ala	Asp	Leu	Pro	Cys 40	Gln	Phe	Ala	Asn	Ser 45	Gln	Asn	Gln
Ser	Leu 50	Ser	Glu	Leu	Val	Val 55	Phe	Trp	Gln	Asp	Gln 60	Glu	Asn	Leu	Val
Leu 65	Asn	Glu	Val	Tyr	Leu 70	Gly	Lys	Glu	Lys	Phe 75	Asp	Ser	Val	His	Ser 80
Lys	Tyr	Met	Gly	Arg 85	Thr	Ser	Phe	Asp	Ser 90	Asp	Ser	Trp	Thr	Leu 95	Arg
Leu	His	Asn	Leu 100	Gln	Ile	Lys	Asp	Lys 105	Gly	Leu	Tyr	Gln	Cys 110	Ile	Ile
His	His	Lys 115	Lys	Pro	Thr	Gly	Met 120	Ile	Arg	Ile	His	Gln 125	Met	Asn	Ser
Glu	Leu 130	Ser	Val	Leu	Ala	Asn 135	Phe	Ser	Gln	Pro	Glu 140	Ile	Val	Pro	Ile
Ser 145	Asn	Ile	Thr	Glu	Asn 150	Val	Tyr	Ile	Asn	Leu 155	Thr	Cys	Ser	Ser	Ile 160
His	Gly	Tyr	Pro	Glu 165	Pro	Lys	Lys	Met	Ser 170	Val	Leu	Leu	Arg	Thr 175	Lys
Asn	Ser	Thr	Ile 180	Glu	Tyr	Asp	Gly	Ile 185	Met	Gln	Lys	Ser	Gln 190	Asp ·	Asn
Val	Thr	Glu 195	Leu	Tyr	Asp	Val	Ser 200	Ile	Ser	Leu	Ser	Val 205	Ser	Phe	Pro
Asp	Val 210	Thr	Ser	Asn	Met	Thr 215	Ile	Phe	Cys	Ile	Leu 220	Glu	Thr	Asp	Lys
Thr 225	Arg	Leu	Leu	Ser	Ser 230	Pro	Phe	Ser	Ile	Glu 235	Leu	Glu	Asp	Pro	Gln 240
Pro	Pro	Pro	Asp	His 245	Ile	Pro	Trp	Ile	Thr 250	Ala	Val	Leu	Pro	Thr 255	Val
Ile	Ile	Cys	Val 260	Met	Val	Phe	Cys	Leu 265	Ile	Leu	Trp	Lys	Trp 270	Lys	Lys
Lys	Lys	Arg 275	Pro	Arg	Asn	Ser	Tyr 280	Lys	Cys	Gly	Thr	Asn 285	Thr	Met	Glu
Arg	Glu 290	Glu	Ser	Glu	Gln	Thr 295	Lys	Lys	Arg	Glu	Lys 300	Ile	His	Ile	Pro
Glu 305	Arg	Ser	Asp	Glu	Ala 310	Gln	Arg	Val	Phe	Lys 315	Ser	Ser	Lys	Thr	Ser 320
Ser	Cys	Asp	Lys	Ser	Asp	Thr	Cys	Phe							

(4) INFORMATION FOR SEQ ID NO:3:

			-	TRANI OPOL				ble									
	(ii) MO	LECU	LE T	YPE:	cDN.	A										
	(ix		A) N.	E: AME/I OCATI			.102	8									
	(xi) SE	QUEN	CE DI	ESCR:	IPTI	ON:	SEQ :	ID N	0:3:							
GGA	GCAA	GCA (GACG	CGTA	AG A	GTGG	CTCC'	r gr	AGGC	AGCA	CGG.	ACTT	GAA	CAAC	CAGAC	Т	60
CCT	GTAG	ACG '	TGTT(CCAG	AA C	rtac:	GGAA(G CA	CCCA		TG G et A						104
				ATG Met													152
				GCT Ala													200
				CCG Pro											CTG Leu 50		248
				GTA Val 55													296
				GGC Gly													342
				AGC Ser													382
				AAG Lys													440
				GGA Gly													488
				AAC Asn 135													536
				TCT Ser													584

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 1151 base pairs(B) TYPE: nucleic acid

								Phe								632
								TCA Ser								680
								CTT Leu								728
								GAA Glu								776
								GAG Glu 235								814
								ACT Thr								872
								AAG Lys								920
								CGG Arg								968
								CCC Pro								1016
	GCA Ala		TGAA	AGGCF	AGT G	SAGAG	CCTC	GA GO	SAAAG	SAGTT	AAA ?	LTAAL	GCT			1065
TTGO	CCTGF	L AA	AAGA	AGTO	C A	SAGTI	TCTC	C AGA	ATTC	AAA	AATO	STTCI	CA C	SCTGF	TTGGA	1115
ATTO	CTACA	AGT I	GAAT	TAAT	'A AA	GAAC	:									1151

(5) INFORMATION FOR SEQ ID NO:4:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 309 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:4:
- Met Asp Pro Arg Cys Thr Met Gly Leu Ala Ile Leu Ile Phe Val Thr
 1 5 10 15
- Val Leu Leu Ile Ser Asp Ala Val Ser Val Glu Thr Gln Ala Tyr Phe 20 25 30
- Asn Gly Thr Ala Tyr Leu Pro Cys Pro Phe Thr Lys Ala Gln Asn Ile $35 \hspace{1cm} 40 \hspace{1cm} 45$
- Ser Leu Ser Glu Leu Val Val Phe Trp Gln Asp Gln Gln Lys Leu Val 50 55 60
- Leu Tyr Glu His Tyr Leu Gly Thr Glu Lys Leu Asp Ser Val Asn Ala 65 70 75 80
- Lys Tyr Leu Gly Arg Thr Ser Phé Asp Arg Asn Asn Trp Thr Leu Arg 85 90 95
- Leu His Asn Val Gln Ile Lys Asp Met Gly Ser Tyr Asp Cys Phe Ile 100 105 110
- Gln Lys Lys Pro Pro Thr Gly Ser Ile Ile Leu Gln Gln Thr Leu Thr 115 120 125
- Glu Leu Ser Val Ile Ala Asn Phe Ser Glu Pro Glu Ile Lys Leu Ala 130 135 140
- Gln Asn Val Thr Gly Asn Ser Gly Ile Asn Leu Thr Cys Thr Ser Lys 145 150 155 160
- Gln Gly His Pro Lys Pro Lys Lys Met Tyr Phe Leu Ile Thr Asn Ser 165 170 175
 - Thr Asn Glu Tyr Gly Asp Asn Met Gln Ile Ser Gln Asp Asn Val Thr 180 185 190
 - Glu Leu Phe Ser Ile Ser Asn Ser Leu Ser Leu Ser Phe Pro Asp Gly
 195 200 205
 - Val Trp His Met Thr Val Val Cys Val Leu Glu Thr Glu Ser Met Lys 210 215 220
 - Ile Ser Ser Lys Pro Leu Asn Phe Thr Gln Glu Phe Pro Ser Pro Gln 225 230 235 240
 - Thr Tyr Trp Lys Glu Ile Thr Ala Ser Val Thr Val Ala Leu Leu Leu 245 250 255
 - Val Met Leu Leu Ile Ile Val Cys His Lys Lys Pro Asn Gln Pro Ser 260 265 270

275	280	-	285	-
Arg Glu Thr Ile Asn L 290	eu Lys Glu Leu 295	Glu Pro Gln 300	Ile Ala Ser	Ala
Lys Pro Asn Ala Glu 305				
(6) INFORMATION FOR	SEQ ID NO:5:			
(i) SEQUENCE C	HARACTERISTICS	:		
(B) TYPE: (C) STRAND	: 1491 base pa nucleic acid EDNESS: double GY: linear			
(ii) MOLECULE	TYPE: cDNA to	mRNA		
(vi) ORIGINAL	SOURCE:			
(F) TISSUE	SM: <u>Homo</u> <u>sapie</u> TYPE: lymphoi YPE: B cell INE: Raji			
(xi) SEQUENCE	DESCRIPTION:	SEQ ID NO:5:		
CCAAAGAAAA AGTGATTTGT	CATTGCTTTA TA	GACTGTAA GAA	GAGAACA TCTC	AGAAGT 60
GGAGTCTTAC CCTGAAATCA	AAGGATTTAA AG	AAAAAGTG GAA	TTTTTCT TCAG	CAAGCT 120
GTGAAACTAA ATCCACAACC	TTTGGAGACC CA	GGAACACC CTC	CAATCTC TGTG	rgttt 180
GTAAACATCA CTGGAGGGTC	TTCTACGTGA GC	AATTGGAT TGT	CATCAGC CCTG	CCTGTT 240
TTGCACCTGG GAAGTGCCCT	GGTCTTACTT GG	GTCCAAAT TGT	IGGCTTT CACT	TTTGAC 300
CCTAAGCATC TGAAGCC ATME	t Gly His Thr			
AAG TGT CCA TAC CTG A Lys Cys Pro Tyr Leu A -20				
TCT CAC TTC TGT TCA G Ser His Phe Cys Ser G -5				
GTG GCA ACG CTG TCC TO Val Ala Thr Leu Ser C				

Arg Pro Ser Asn Thr Ala Ser Lys Leu Glu Arg Asp Ser Asn Ala Asp

						ATG Met			545
						AAG Lys			593
						CTG Leu 70			641
						AAG Lys			689
						TTA Leu			737
						ATT Ile			785
						TTT Phe			833
						GCC Ala 150			881
						GTT Val			929
						TGT Cys			977
						AAT Asn			1025

GAG CAT TTT CCT GAT AAC CTG CTC CCA TCC TGG GCC ATT ACC TTA ATC 1073

Glu His Phe Pro Asp Asn Leu Leu Pro Ser Trp Ala Ile Thr Leu Ile 205 210 215	
TCA GTA AAT GGA ATT TTT GTG ATA TGC TGC CTG ACC TAC TGC TTT GCC 1121 Ser Val Asn Gly Ile Phe Val Ile Cys Cys Leu Thr Tyr Cys Phe Ala 220 225 230	
CCA AGA TGC AGA GAG AGA AGG AGG AAT GAG AGA TTG AGA AGG GAA AGT Pro Arg Cys Arg Glu Arg Arg Arg Asn Glu Arg Leu Arg Arg Glu Ser 235 240 245 250	
GTA CGC CCT GTA TAACAGTGTC CGCAGAAGCA AGGGGCTGAA AAGATCTGAA 1221 Val Arg Pro Val	
GGTAGCCTCC GTCATCTCTT CTGGGATACA TGGATCGTGG GGATCATGAG GCATTCTTCC 1281	
CTTAACAAAT TTAAGCTGTT TTACCCACTA CCTCACCTTC TTAAAAACCT CTTTCAGATT 1341	
AAGCTGAACA GTTACAAGAT GGCTGGCATC CCTCTCCTTT CTCCCCATAT GCAATTTGCT 1401	
TAATGTAACC TCTTCTTTTG CCATGTTTCC ATTCTGCCAT CTTGAATTGT CTTGTCAGCC 1461	
AATTCATTAT CTATTAAACA CTAATTTGAG	1491
 (7) INFORMATION FOR SEQ ID NO:6: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 288 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: protein 	

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:6:

Met Gly His Thr Arg Arg Gln Gly Thr Ser Pro Ser Lys Cys Pro Tyr -30

Leu Asn Phe Phe Gln Leu Leu Val Leu Ala Gly Leu Ser His Phe Cys -15

Ser Gly Val Ile His Val Thr Lys Glu Val Lys Glu Val Ala Thr Leu 10

Ser Cys Gly His Asn Val Ser Val Glu Glu Leu Ala Gln Thr Arg Ile 15 20 25 30

Tyr Trp Gln Lys Glu Lys Lys Met Val Leu Thr Met Met Ser Gly Asp Met Asn Ile Trp Pro Glu Tyr Lys Asn Arg Thr Ile Phe Asp Ile Thr 50 55 Asn Asn Leu Ser Ile Val Ile Leu Ala Leu Arg Pro Ser Asp Glu Gly Thr Tyr Glu Cys Val Val Leu Lys Tyr Glu Lys Asp Ala Phe Lys Arg 85 Glu His Leu Ala Glu Val Thr Leu Ser Val Lys Ala Asp Phe Pro Thr 100 105 Pro Ser Ile Ser Asp Phe Glu Ile Pro Thr Ser Asn Ile Arg Arg Ile 115 120 Ile Cys Ser Thr Ser Gly Gly Phe Pro Glu Pro His Leu Ser Trp Leu 135 Glu Asn Gly Glu Glu Leu Asn Ala Ile Asn Thr Thr Val Ser Gln Asp 150 Pro Glu Thr Glu Leu Tyr Ala Val Ser Ser Lys Leu Asp Phe Asn Met Thr Thr Asn His Ser Phe Met Cys Leu Ile Lys Tyr Gly His Leu Arg 175 185 180 Val Asn Gln Thr Phe Asn Trp Asn Thr Thr Lys Gln Glu His Phe Pro 195 200 Asp Asn Leu Leu Pro Ser Trp Ala Ile Thr Leu Ile Ser Val Asn Gly 210 215 Ile Phe Val Ile Cys Cys Leu Thr Tyr Cys Phe Ala Pro Arg Cys Arg 230 Glu Arg Arg Arg Asn Glu Arg Leu Arg Arg Glu Ser Val Arg Pro Val

(8) INFORMATION FOR SEQ ID NO:7:

240

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 1716 base pairs

245

- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear
- (ii) MOLECULAR TYPE: cDNA to mRNA
- (vi) ORIGINAL SOURCE:

- (A) ORGANISM: <u>Mus</u> <u>musculus</u>(D) DEVELOPMENTAL STAGE: germ line
- (F) TISSUE TYPE: lymphoid(G) CELL TYPE: B lymphocyte (H) CELL LINE: 70Z and A20

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:7:

GAG:	TTTT	ATA	CCTC	ATAA	GA C	rctt/	ACTA(G TT	rctc'	гттт	TCA	GGTT	GTG A	AAAC'	TCAACC	60
TTC	AAAG	ACA (CTCT	GTTC	CA T	TTCT	GTGG	A CTA	ATA	GGAT	CAT	CTTT	AGC A	ATCT	GCCGGG	120
TGG	ATGC	CAT (CCAG	GCTT(CT T	TTTC	raca:	r cro	CTGT	rtct	CGA'	rttt'	rgț (GAGC	CTAGGA	180
GGT	GCCTA	AAG (CTCC	ATTG	GC TO	CTAGA	ATTCO	C TG	GCTT'	rccc	CAT	CATG'	TTC '	rcca.	AAGCAT	240
CTGAAGCT ATG GCT TGC AAT TGT CAG TTG ATG CAG GAT ACA CCA CTC CTC Met Ala Cys Asn Cys Gln Leu Met Gln Asp Thr Pro Leu Leu -35 -30 -25															290	
				CCA Pro												338
				TCT Ser												386
				TTG Leu												434
				CGA Arg 30												482
				GGG Gly												530
				AAC Asn												578
				GGC Gly												626
				GTT Val												674

GCT GAC TTC TCT ACC CCC AAC ATA ACT GAG TCT GGA AAC CCA TCT GCA Ala Asp Phe Ser Thr Pro Asn Ile Thr Glu Ser Gly Asn Pro Ser Ala 110 115 120	22
GAC ACT AAA AGG ATT ACC TGC TTT GCT TCC GGG GGT TTC CCA AAG CCT Asp Thr Lys Arg Ile Thr Cys Phe Ala Ser Gly Gly Phe Pro Lys Pro 125 130 135	70
CGC TTC TCT TGG TTG GAA AAT GGA AGA GAA TTA CCT GGC ATC AAT ACG Arg Phe Ser Trp Leu Glu Asn Gly Arg Glu Leu Pro Gly Ile Asn Thr 140 145 150	18
ACA ATT TCC CAG GAT CCT GAA TCT GAA TTG TAC ACC ATT AGT AGC CAA Thr Ile Ser Gln Asp Pro Glu Ser Glu Leu Tyr Thr Ile Ser Ser Gln 155 160 165	66
CTA GAT TTC AAT ACG ACT CGC AAC CAC ACC ATT AAG TGT CTC ATT AAA 91 Leu Asp Phe Asn Thr Thr Arg Asn His Thr Ile Lys Cys Leu Ile Lys 170 185	14
TAT GGA GAT GCT CAC GTG TCA GAG GAC TTC ACC TGG GAA AAA CCC CCA Tyr Gly Asp Ala His Val Ser Glu Asp Phe Thr Trp Glu Lys Pro Pro 190 195 200	62
GAA GAC CCT CCT GAT AGC AAG AAC ACA CTT GTG CTC TTT GGG GCA GGA Glu Asp Pro Pro Asp Ser Lys Asn Thr Leu Val Leu Phe Gly Ala Gly 205 210 215	10
TTC GGC GCA GTA ATA ACA GTC GTC GTC ATC GTT GTC ATC ATC AAA TGC Phe Gly Ala Val Ile Thr Val Val Val Ile Val Val Ile Ile Lys Cys 220 230	58
TTC TGT AAG CAC AGA AGC TGT TTC AGA AGA AAT GAG GCA AGC AGA GAA 110 Phe Cys Lys His Arg Ser Cys Phe Arg Arg Asn Glu Ala Ser Arg Glu 235 240 245	3 6
ACA AAC AAC AGC CTT ACC TTC GGG CCT GAA GAA GCA TTA GCT GAA CAG Thr Asn Asn Ser Leu Thr Phe Gly Pro Glu Glu Ala Leu Ala Glu Gln 250 265	54
ACC GTC TTC CTT TAGTTCTTCT CTGTCCATGT GGGATACATG GTATTATGTG Thr Val Phe Leu 12	206
GCTCATGAGG TACAATCTTT CTTTCAGCAC CGTGCTAGCT GATCTTTCGG ACAACTTGAC 126	56
ACAAGATAGA GTTAACTGGG AAGAGAAAGC CTTGAATGAG GATTTCTTTC CATCAGGAAG 132	26
CTACGGGCAA GTTTGCTGGG CCTTTGATTG CTTGATGACT GAAGTGGAAA GGCTGAGCCC 138	36
ACTGTGGGTG GTGCTAGCCC TGGGCAGGGG CAGGTGACCC TGGGTGGTAT AAGAAAAAGA 144	16
GCTGTCACTA AAAGGAGAGG TGCCTAGTCT TACTGCAACT TGATATGTCA TGTTTGGTTG 150)6
GTGTCTGTGG GAGGCCTGCC CTTTTCTGAA GAGAAGTGGT GGGAGAGTGG ATGGGGTGGG 156	56
GGCAGAGGAA AAGTGGGGGA GAGGGCCTGG GAGGAGAGGA	26
GTGGGGAAAA CTATGGTTGG GATGTAAAAA CGGATAATAA TATAAATATT AAATAAAAAG 168	36

- (9) INFORMATION FOR SEQ ID NO:8:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 306 amino acids
 - (B) TYPE: amino acid
 - (C) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: protein
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:8:
- Met Ala Cys Asn Cys Gln Leu Met Gln Asp Thr Pro Leu Leu Lys Phe
 -35 -30 -25
- Pro Cys Pro Arg Leu Ile Leu Leu Phe Val Leu Leu Ile Arg Leu Ser -20 -15 -10
- Gln Val Ser Ser Asp Val Asp Glu Gln Leu Ser Lys Ser Val Lys Asp
 -5 -1 1 5 10
- Lys Val Leu Leu Pro Cys Arg Tyr Asn Ser Pro His Glu Asp Glu Ser 15 20 25
- Glu Asp Arg Ile Tyr Trp Gln Lys His Asp Lys Val Val Leu Ser Val 30 35 40
- Ile Ala Gly Lys Leu Lys Val Trp Pro Glu Tyr Lys Asn Arg Thr Leu
 45 50 55
- Tyr Asp Asn Thr Tyr Ser Leu Ile Ile Leu Gly Leu Val Leu Ser 60 65 70 75
- Asp Arg Gly Thr Tyr Ser Cys Val Val Gln Lys Lys Glu Arg Gly Thr 80 85 90
- Tyr Gly Val Lys His Leu Ala Leu Val Lys Leu Ser Ile Lys Ala Asp 95 100 105
- Phe Ser Thr Pro Asn Ile Thr Glu Ser Gly Asn Pro Ser Ala Asp Thr 110 115 120
- Lys Arg Ile Thr Cys Phe Ala Ser Gly Gly Phe Pro Lys Pro Arg Phe 125 130 135
- Ser Trp Leu Glu Asn Gly Arg Glu Leu Pro Gly Ile Asn Thr Thr Ile 140 145 150 155
- Ser Gln Asp Pro Glu Ser Glu Leu Tyr Thr Ile Ser Ser Gln Leu Asp 160 165 170
- Phe Asn Thr Thr Arg Asn His Thr Ile Lys Cys Leu Ile Lys Tyr Gly 175 180 185

Asp Ala His Val Ser Glu Asp Phe Thr Trp Glu Lys Pro Pro Glu Asp 190 195 200

Pro Pro Asp Ser Lys Asn Thr Leu Val Leu Phe Gly Ala Gly Phe Gly 205 210 215

Ala Val Ile Thr Val Val Val Ile Val Val Ile Ile Lys Cys Phe Cys 220 225 230 235

Lys His Arg Ser Cys Phe Arg Arg Asn Glu Ala Ser Arg Glu Thr Asn 240 245 250

Asn Ser Leu Thr Phe Gly Pro Glu Glu Ala Leu Ala Glu Gln Thr Val 255 260 265

Phe Leu